

REMARKS


Claims 2, to 5, 10, 14, 16 to 18, 20 to 22, 26 to 28, 31, 34, 37, 39, 40, 50, 55 and 56 and new Claims 57 and 58 are present.

Basis for the amendment to Claim 37 and new Claims 57 and 58 is found in the Specification at page 81, lines 17 to 22 and page 84, lines 22 to 29.

It is believed that the subject application is in good form for examination.

Respectfully submitted,

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336



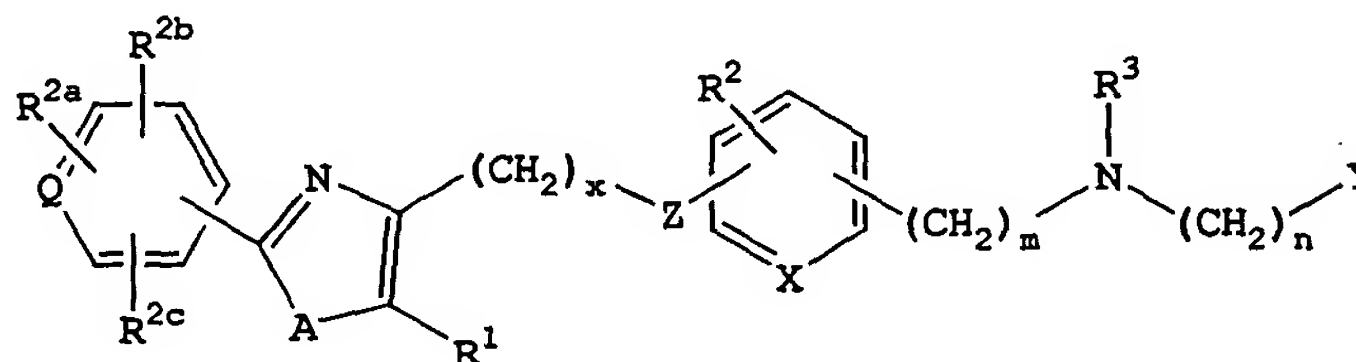
Burton Rodney
Attorney for Applicants
Reg. No. 22,076

Date: Oct. 24, 2002

MARKED UP COPY TO SHOW CHANGES

Please amend Claim 37 to read as follows:

-- 37. (Twice Amended) A pharmaceutical combination comprising a compound which has the structure



wherein x is 1, 2, 3 or 4; m is 1 or 2; n is 1 or 2;

Q is C or N;

A is O or S;

Z is O or a bond;

R¹ is H or lower alkyl;

X is CH;

R² is H, alkyl, alkoxy, halogen, amino or substituted amino;

R^{2a}, R^{2b} and R^{2c} are the same or different and are selected from H, alkyl, alkoxy, halogen, amino or substituted amino;

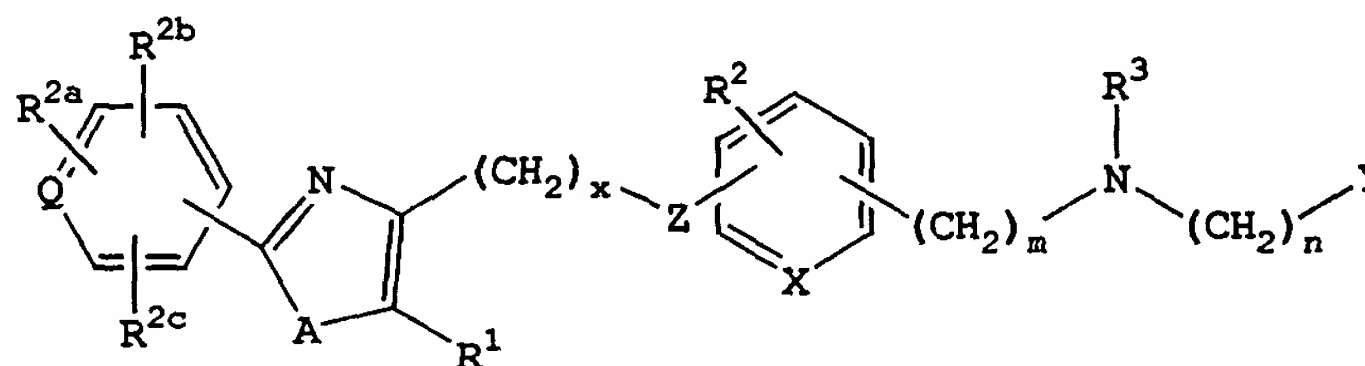
R³ is aryloxy carbonyl, alkyloxy carbonyl, alkynyloxy carbonyl, alkenyloxy carbonyl, alkyl(halo)aryloxy carbonyl, alkyloxy(halo)aryloxy carbonyl, cycloalkylaryloxy carbonyl, cycloalkyloxyaryloxy carbonyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxy carbonylamino, aryloxy carbonylamino, heteroaryloxy carbonylamino, alkylsulfonyl, alkenylsulfonyl, heteroaryloxy carbonyl, cycloheteroalkyloxy carbonyl, heteroarylalkenyl, hydroxyalkyl, alkoxy, alkoxyaryloxy carbonyl, arylalkyloxy carbonyl, alkylaryloxy carbonyl, alkynyloxy carbonyl, haloalkoxyaryloxy carbonyl, alkoxy carbonylaryloxy carbonyl, aryloxyaryloxy carbonyl, arylalkenyloxy carbonyl, heteroaryloxyarylalkyl, aryloxyarylalkyloxy carbonyl, aryloxyalkyloxy carbonyl, arylalkylsulfonyl, arylthiocarbonyl, arylalkenylsulfonyl, heteroarylsulfonyl, arylsulfonyl, heteroarylalkoxy carbonyl, heteroarylalkyloxyarylalkyl, arylalkenylarylalkyl, arylalkoxy carbonyl(heteroarylalkyl), heteroaryloxyarylalkyl, arylalkenylheteroarylalkyl or polyhaloalkylaryloxy carbonyl;

Y is CO₂R⁴ where R⁴ is H or alkyl, or a prodrug ester or Y is a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR^{4a})R⁵ where R^{4a} is H or a prodrug ester, R⁵ is alkyl or aryl or a phosphonic acid of the structure P(O)(OR^{4a})₂ where R^{4a} is H or a prodrug ester;

or stereoisomers thereof, prodrug esters thereof, and pharmaceutically acceptable salts thereof, and a lipid-lowering agent, a lipid modulating agent, an antidiabetic agent, an anti-obesity agent, an antihypertensive agent which is other than a diuretic, a platelet aggregation inhibitor, and/or an antiosteoporosis agent. --

Please add Claims 57 and 58 as set out below.

-- 57. A pharmaceutical combination comprising a compound which has the structure



wherein x is 1,2, 3 or 4; m is 1 or 2; n is 1 or 2;

Q is C or N;

A is O or S;

Z is O or a bond;

R¹ is H or lower alkyl;

X is CH;

R² is H, alkyl, alkoxy, halogen, amino or substituted amino;

R^{2a}, R^{2b} and R^{2c} are the same or different and are selected from H, alkyl, alkoxy, halogen, amino or substituted amino;

R³ is aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, alkyl(halo)aryloxycarbonyl, alkyloxy(halo)aryloxycarbonyl, cycloalkylaryloxycarbonyl, cycloalkyloxyaryloxycarbonyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxy carbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkenyl, hydroxyalkyl, alkoxy, alkoxyaryloxycarbonyl, arylalkyloxycarbonyl, alkylaryloxycarbonyl, alkynyloxycarbonyl, haloalkoxyaryloxycarbonyl, alkoxy carbonylaryloxycarbonyl, aryloxyaryloxycarbonyl, arylalkenyloxycarbonyl, heteroaryloxyarylalkyl, aryloxyarylalkyloxycarbonyl, aryloxyalkyloxycarbonyl, arylalkylsulfonyl, arylthiocarbonyl, arylalkenylsulfonyl, heteroarylsulfonyl, arylsulfonyl, heteroarylalkoxycarbonyl, heteroarylalkyloxyarylalkyl, arylalkenylarylalkyl, arylalkoxycarbonylheteroarylalkyl, heteroaryloxyarylalkyl, arylalkenylheteroarylalkyl or polyhaloalkylaryloxycarbonyl;

Y is CO_2R^4 where R^4 is H or alkyl, or a prodrug ester or Y is a C-linked 1-tetrazole, a phosphinic acid of the structure $\text{P}(\text{O})(\text{OR}^{4a})\text{R}^5$ where R^{4a} is H or a prodrug ester, R^5 is alkyl or aryl or a phosphonic acid of the structure $\text{P}(\text{O})(\text{OR}^{4a})_2$ where R^{4a} is H or a prodrug ester;

or stereoisomers thereof, prodrug esters thereof, and pharmaceutically acceptable salts thereof, and an antihypertensive agent which is a diuretic. --

-- 58. The combination as defined in Claim 57 wherein the diuretic is hydrochlorothiazide, torasemide, furosemide, spironolactone or indapamide. --